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ACUTE TOXICITY OF THIONYL CHLORIDE VAPOR FOR RATS

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TECHNICAL REVIEW AND APPROVAL

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The experiments reported herein were conducted according to the "Guide for the Care and Use of Laboratory Animals," Institute of Laboratory Animal Resources, National Research Council.

This report has been reviewed by the Office of Public Affairs (PA) and is releasable to the National Technical Information Service (NTIS). At NTIS, it will be available to the general public, including foreign nations.

This technical report has been reviewed and is approved for publication.

FOR THE COMMANDER



BRUCE O. STUART, PhD
Director Toxic Hazards Division
Air Force Aerospace Medical Research Laboratory

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<p>Rats were exposed to thionyl chloride vapor for one hour to determine the acute inhalation toxicity of this compound. The thionyl chloride was completely hydrolyzed to sulfur dioxide and hydrogen chloride gases when evaporated in air. The calculated LD₅₀ expressed as thionyl chloride was 500 ppm for a one hour single exposure and the acute toxicity of the hydrolyzed mixture was comparable to a theoretical calculation for additive effects of the mixture. The acute toxicity of thionyl chloride appears to be much lower than previously reported.</p>					
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PREFACE

This report on the acute toxicity of thionyl chloride is one of a series of technical reports describing the results of the experimental laboratory program being conducted in the Toxic Hazards Research Unit (THRU). The experimental program has been accomplished on behalf of the Air Force by the University of California, Irvine under contract #F3361580-C-0512 from June 1984 through September 1984. M. K. Pinkerton served as contract technical monitor for the Air Force Aerospace Medical Research Laboratory.

J. D. MacEwen, Ph.D. served as Laboratory Director for the THRU of the University of California, Irvine and as co-principal investigator with T. T. Crocker, M.D., Professor, Department of Community and Environmental Medicine. Acknowledgement is made to R. Scott Bowers and R. Blasingame for their significant contributions and assistance in the preparation of this report.

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INTRODUCTION

The Air Force will be replacing existing standby power batteries at Minuteman Missile sites with new lithium/thionyl chloride batteries. During use, storage, or deactivation of lithium batteries, thionyl chloride may be released into the environment.

Little information is available on the toxicity of thionyl chloride. Generally, thionyl chloride (SOCl_2) vapor is thought to decompose in moist air to form hydrogen chloride and sulfur dioxide. For this reason, the toxic effect of thionyl chloride is often assumed as the additive effect of hydrogen chloride and sulfur dioxide. Patty (1963) mentions a study by Flury and Zernik (1931) in which a 20-minute exposure to 17.5 ppm thionyl chloride proved fatal to cats. However, there appears to be an error in the original publication in conversion of units which leads to uncertainty in the actual concentration tested.

Studies have been conducted in this laboratory on the acute toxicity of hydrogen chloride and sulfur dioxide. Darmer et al. (1972) reported a five-minute and thirty-minute male rat LC_{50} for hydrogen chloride vapor of 40,898 and 4,701 ppm, respectively. MacEwen and Vernot (1976) report a one-hour rat LC_{50} of 3120 ppm for hydrogen chloride vapor. The one-hour inhalation LC_{50} value of sulfur dioxide vapor for male rats has been reported by MacEwen and Vernot (1977) as 2520 ppm.

This study was designed to determine the male rat one-hour LC_{50} of thionyl chloride when delivered to an exposure chamber in an atmosphere of low humidity which would result in minimum decomposition of the contaminant. It was also our purpose to determine whether the acute toxicity of thionyl chloride could be considered as the additive effect of its decomposition products.

METHODS AND MATERIALS

Test Agent

Thionyl chloride was purchased from Aldrich Chemical Company, Milwaukee, Wisconsin. Properties and specifications of this test agent are as follows:

Cas. No.:	7719-09-7
Grade:	99 + % purity (gold label)
Cat. No.:	23,046-4
Molecular Weight:	118.97
Boiling Point:	75.5°C
Density:	1.64 g/cc
Vapor Pressure:	110 mm Hg @ 26°C
Appearance:	liquid, clear to slightly yellow

Quality control analyses on SOCl_2 were conducted using a Beckman Acculab 4, infrared (IR) analyzer. IR scans were obtained for approximately 10 mg/mL concentrations of SOCl_2 in carbon tetrachloride which were read against a solvent blank.

Sample and blank were placed in Beckman, variable path length, liquid cells (Model #29896) adjusted to matching path lengths of 0.10 mm. Both QC scans agreed with the SOCl_2 IR spectrum (#1336) in the Stadler Index.

Generation

Exposures were conducted in a 60-liter, Plexiglas®, exposure chamber. The chamber air supply consisted of high purity dry nitrogen (99.99% min., Matheson Gas Products) and Zero-Gas® dry oxygen (99.8% min., Matheson Gas Products) combined in a 4:1 flow ratio monitored with calibrated, Fischer & Porter flowmeters. High purity dry gases were used to minimize hydrolytic decomposition of thionyl chloride. The combined nitrogen and oxygen flow was set at 30 liters per minute. Exposure chamber air was exhausted through a scrubber and discharged into the atmosphere.

Liquid thionyl chloride was supplied by a syringe pump (Sage, Model 355) to a helical, glass evaporating tower where it was vaporized in a counterstream of nitrogen. Because of SOCl_2 volatility and the possibility of thermal decomposition, the evaporating tower was not heated. Figure 1 is a schematic diagram of the chamber and contaminant introduction system.

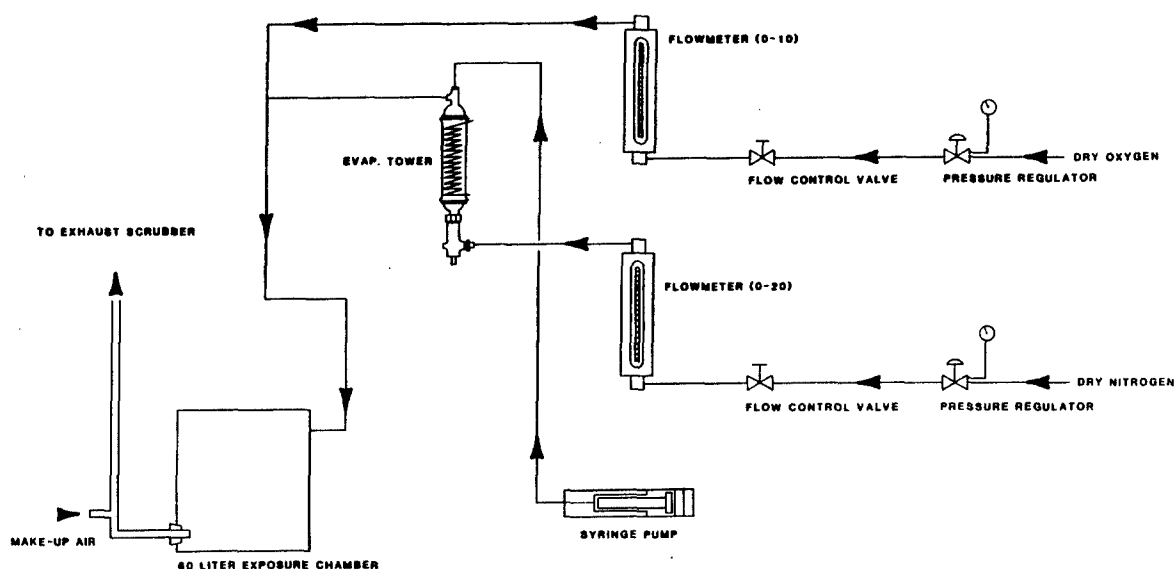


Figure 1. Chamber and contaminant introduction system for thionyl chloride, LC_{50} study.

Total Chloride Contaminant Analysis

The analytical system is illustrated in Figure 2. The chamber atmosphere was drawn through a helical, absorber tower (1/4" I.D. glass, 5-turn, 1-1/2" diameter spiral, bead-filled) by a double-diaphragm vacuum pump with a contiguous flow of aqueous, absorbing solution supplied by a peristaltic pump. The ratio of chamber air to absorbing liquid flow was 1000:1. An air flow of 2.0 L/min. through the tower was monitored continuously during the exposures with a calibrated, Fischer & Porter flowmeter. The tower liquid flow was adjusted to 2.0 mL/min. prior to each exposure. Complete transfer of contaminant from the vapor to aqueous phase was obtained at this ratio using chloride ion as the measured species.

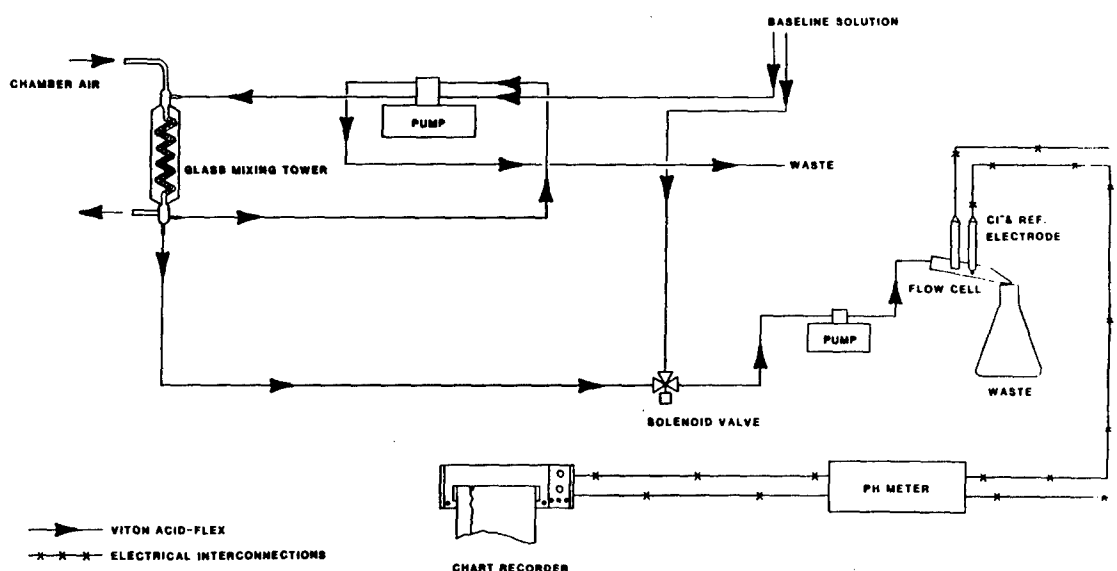


Figure 2. Analysis system for total chloride contaminants, thionyl chloride LC50 study.

A second Polystaltic pump transmitted the aqueous, tower effluent to a flow cell containing a chloride ion electrode (Orion, Model #94-17B) and a reference electrode (Orion, Model #90-02). Electrode response was read on a pH meter set on expanded millivolt scale and referenced to a strip-chart recorder. A timer-controlled, electromechanical valve switched from tower effluent to baseline absorbing solution from a tower by-pass.

The chloride ion electrode response was calibrated using aqueous chloride standards prepared by volumetric dilution of 1 M NaCl (aq) with 1 M KNO₃ (aq). This diluent was used to provide constant ionic strength for all chloride standards enabling the electrode response to be concentration dependent rather than

activity dependent. Standard chloride solutions employed for instrument calibration ranged in concentration from 0.050 M Cl^- to 0.50 M Cl^- .

Thionyl Chloride Analysis

The concentration of unhydrolyzed SOCl_2 in the chamber atmosphere was measured by IR analysis of carbon tetrachloride (CCl_4) solutions of the contaminant obtained by impinger sampling. Chamber air was drawn through a train of three impingers, each containing 20 mL of CCl_4 , at a metered flow of 1.5 L/min. The resultant solutions were read on the Beckman Acculab 4 IR analyzer against a CCl_4 blank using liquid cells with sodium chloride windows and set at 0.1 mm path lengths. The instrument scanned each impinger sample from a wavelength of 2.5 μm to 16 μm . Absorbance at 8.3 μm was indicative of SOCl_2 .

The instrument was calibrated by measuring the absolute transmittance at 8.3 μm of standard solutions of SOCl_2 dissolved in CCl_4 . Transmittance was converted to absorbance units and plotted as a function of standard concentration in mg/mL.

Sampling for thionyl chloride analysis was done once during each exposure. The chamber was allowed to achieve a stable total chloride contaminant concentration as indicated by the chloride ion electrode analysis before impinger sampling was initiated. In most cases, impinger sampling continued for the duration of the exposure.

Animals

The animals used in these experiments were male CDF® (Fischer 344)/CrlBR rats, nine to eleven weeks of age, obtained from Charles River Breeding Labs, Wilmington, Massachusetts. Exposure groups consisted of five animals. Quality control studies on the rats during the quarantine period showed the animals to be in good health.

EXPERIMENTAL RESULTS

Calculations

The results of chloride ion analysis were calculated as the concentration of SOCl_2 in the chamber assuming no aqueous decomposition of the test agent took place. However, extensive decomposition of SOCl_2 did occur, so these concentrations served only as a means for computing stoichiometrically the product concentrations. The calculation for chamber concentration of chloride contaminant as SOCl_2 is as follows:

$$\text{Molarity Cl}^- (\text{aq}) \times \frac{1 \text{ mol SOCl}_2}{2 \text{ mol Cl}^-} \times \frac{1 \text{ mL}}{1000 \text{ mL}} \times 24.5 \times 10^6 = \text{ppm SOCl}_2 \quad (1)$$

For IR analysis of SOCl₂ actually present in the chamber, the concentration of this contaminant in mg/mL for each impinger was calculated from a calibration curve. Concentrations of the impinger samples were multiplied by their respective solution volumes (mL) after sampling and summed to yield total SOCl₂ in milligrams. The calculation of chamber concentration of SOCl₂ then proceeded as follows:

$$\text{mg SOCl}_2 \times \frac{1}{T_s (\text{min})} \times \frac{1 \text{ min}}{1.5 \text{ L}} \times \frac{1000 \text{ L}}{\text{m}^3} \times \frac{1 \text{ ppm}}{4.87 \text{ mg/m}^3} = \text{ppm SOCl}_2 \quad (2)$$

where T_s is the duration of the sampling interval.

The stoichiometry of SOCl₂ decomposition in the chamber is given by the following equation:



Results

The concentrations of decomposed and undecomposed SOCl₂ determined during the inhalation exposures are given in Table 1. Although dry gases were used to generate the atmospheres, enough moisture was produced by the rats to produce relative humidities of around 50%. Under these conditions, SOCl₂ was completely hydrolyzed, or almost so, in all experiments so that rats were exposed to SO₂ and HCl in a ratio of 1:2.

TABLE 1. CONCENTRATIONS OF DECOMPOSED AND UNDECOMPOSED THIONYL CHLORIDE IN INHALATION EXPOSURE CHAMBERS

<u>Decomposed Conc., ppm</u>	<u>SD ppm</u>	<u>Undecomposed Conc., ppm</u>	<u>Chamber Temp., °C</u>	<u>% Rel. Humidity</u>
661	± 68	11	22.0	47
503	± 46	0	25.0	39
413	± 24	0	23.5	46
360	±110 ^a	0	27.0	58
302	± 44	0	25.0	50

^a Large standard deviation due to syringe pump jamming during exposure.

Mortality in the one-hour inhalation exposures is shown in Table 2. Low non-lethal concentrations were irritating to the eyes and respiratory system resulting in shallow breathing and, eventually, gasping. Deaths were directly attributed to severe lung irritation with resultant edema formation. Deaths usually occurred within 24 hours of exposure termination. No deaths occurred beyond 48 hours after exposure.

Survivors of lethal concentrations never regained original body weight, with the exception of the single survivor from the highest concentration exposure. Rats exposed at non-lethal concentrations did not regain their original body weight until the second week of postexposure observation.

TABLE 2. RESULTS OF ONE-HOUR INHALATION EXPOSURES OF MALE FISCHER 344 RATS TO THIONYL CHLORIDE

Concentration, ppm ^a				Mortality Ratio	Time of Death (No/Day)	
SOCl ₂	SO ₂	HCl	SO ₂ -HCl Total		1	2
11	661	1322	1983	4/5	3	1
0	503	1006	1509	3/5	3	-
0	413	826	1239	2/5	2	-
0	360	720	1080	0/5	-	-
0	302	604	906	0/5	-	-

^a SOCl₂ measured concentrations, others calculated.

LC₅₀ of SO₂ + HCl mixture (95% confidence limits) = 1480 (1170-2110) ppm.

LC₅₀ calculated as SOCl₂ (95% confidence limits) = 500 (420-660) ppm.

Pathology

Gross examination of the rats that died during or shortly following exposure showed that the respiratory tract was the primary target for the SOCl₂ damage. Mild to moderate multifocal congestion with multiple areas of moderate to severe ecchymotic hemorrhage were observed in the rats. There was also evidence of atelectasis and consolidation with some residual alveolar damage.

DISCUSSION

The acute effects of exposure to SOCl₂ were similar to those observed with exposure to other pulmonary irritants such as OF₂ (Davis, 1970), HF (DiPasquale and Davis, 1971), ClF₃ (Darmer, 1971), CF₃ (Dost et al., 1967), and HCl (Darmer et al., 1972).

Deaths were attributed primarily to the irritative effects of the compound on the respiratory tract.

The exposures of male rats to SOCl_2 were carried out by generating the contaminant in very dry air to minimize decomposition. However, it was impossible to eliminate all water from the exposure chamber due to the moisture from the animals breath and excreta. Except for one exposure, the complete breakdown of SOCl_2 to SO_2 and HCl was not prevented.

Finney (1952) gives the following equation for calculation of mixture LC_{50} values:

$$\frac{1}{\text{Predicted } \text{LC}_{50} \text{ Mixture}} = \frac{p_a}{\text{LC}_{50} \text{ Component}_a} + \frac{p_b}{\text{LC}_{50} \text{ Component}_b} \quad (4)$$

Where: p_a = Proportion of component a, p_b = Proportion of component b and $p_a + p_b = 1.00$.

For the 1:2 mixture of SO_2 and HCl , this becomes:

$$\frac{1}{\text{LC}_{50} \text{ Mixture}} = \frac{0.33}{2520} + \frac{0.67}{3120} \quad (5)$$

Predicted LC_{50} mixture = 2890 ppm or 960 ppm as SOCl_2 .

Since the measured LC_{50} of the mixture was 1480 ppm, or 500 ppm as SOCl_2 , the acute toxicity of the mixture is greater than would be expected from simple additivity but not enough to place it in a higher toxicity class. Moreover, the major reason for measuring the acute toxicity of SOCl_2 was that Flury and Zernik (1931) stated that cats were killed during a 20-minute inhalation exposure to 17.5 ppm, a value which appears to be in error. Our data obtained with rats demonstrate that SOCl_2 is not extremely toxic.

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